REMARKS

Applicant has amended claims 1, 2, 5, 6, 43, 49-54, 56-59, 91, 93, and 94, and have canceled claims 3, 4, 7-42, 44, 47, 48 and 55-60, during prosecution of this patent application. Applicants are not conceding in this patent application that said amended and canceled claims are not patentable over the art cited by the Examiner, since the claim amendments and cancellations are only for facilitating expeditious prosecution of this patent application. Applicant respectfully reserves the right to pursue said amended and canceled claims, and other claims, in one or more continuations and/or divisional patent applications.

The amendment to the specification corrects a typographical error and does not add new matter.

The Examiner objected to claim 54.

The Examiner rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Examiner rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner rejected claims 2, 5 and 6 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner rejected claims 1, 2, 5, 6, 43 and 91-94 under 35 U.S.C. § 102(b) as allegedly being anticipated by Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892).

The Examiner rejected claims 1, 43, 49 and 50 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Weitz et al. (US Patent 6,075,013, issued 13 Jun 2000, of record).

The Examiner rejected claims 1 and 56-59 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Conrad et al. (US Patent 5,280,016, issued 18 Jan 1994, cited in PTO-892).

The Examiner rejected claims 1, 43 and 51-54 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Conrad et al. (US Patent 5,280,016, issued 18 Jan 1994, cited in PTO-892) as applied to claims 1 and 56-59 above, and further in view of Kerbel et al. (Cancer and Metastasis Reviews, 2001, 20, p79-86, cited in PTO-892).

The Examiner rejected claims 1, 56, 61 and 62 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Scholander (US Patent 6,461,665, issued 08 Oct 2002, of record).

Applicant respectfully traverses the claim objection, § 112, § 102 and 103 rejections with the following arguments.

Claim Objection

The Examiner objected to claim 54. The Examiner argues: "Claim 54 is objected to because of the following informalities: minor typographical errors, such as "thiotepa", presumably referring to the compound thioTEPA, and "no classic alkylators", which may refer to non-classic alkylators or any agent that is not a classic alkylator. Appropriate correction is required."

In response, Applicant has corrected a typographical error by changing "no classic alkylators" to "non-classic alkylators".

In further response, Applicant respectfully note that the cytotoxic or chemotherapeutic agent referred to in claim 54 by the Examiner is not "thiotepa" but rather is "aziridine thiotepa".

Accordingly, Applicant respectfully requests that the objection to claim 54 be withdrawn.

35 U.S.C. § 112, First Paragraph

Enablement

The Examiner rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner argues that the recitation of "to fully inhibit angiogenesis" is not enabled by the specification.

In response, Applicant has amended claim 1 to replace "to fully inhibit angiogenesis" with "to fully inhibit fibroblast growth factor (FGF2) induced angiogenesis" which is supported in Table 3 on page 29 of Applicant's specification. Table 3 shows that the FGF2 + super-sulphated oxidized ultra-LMWH reduces the FGF2-stimulated cell tube formation from 79.83 to 40.20 which is at the level of the control (PBS) of 41.36, so that the FGF2 + super-sulphated oxidized ultra-LMWH fully inhibits FGF2 induced angiogenesis.

Additional support for full inhibition of FGF2 induced angiogenesis by the super-sulphated oxidized ultra-LMWH of the present invention is provided by Table 4 on page 30 of Applicant's specification. Table 4 shows that the FGF2 + super-sulphated oxidized ultra-LMWH reduces the FGF2-stimulated number of vessel branch points in a circular region equal to the area of a FGF2-saturated filter disk from 264 to 90 ± 8 which is at the level of the control (PBS) of 95 ± 11, so that the FGF2 + super-sulphated oxidized ultra-LMWH fully inhibits FGF2 induced angiogenesis.

Based on the preceding argument, Applicant respectfully requests that the rejection of claim 1 on the ground of allegedly failing to comply with the enablement requirement be withdrawn.

Written Description

The Examiner rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner argues: "Amended claim 1 recites the limitation, "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been 0-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction." The ordinary definition of vertex is a corner of a polygon; as anhydroglucose is usually drawn as a hexagon, this is interpreted to mean 0-sulfation at the oxygen at each corner, or carbon, of the anhydroglucose unit. However, no support for this specific limitation can be found in the application as filed or in the parentprovisional application 60/411,851 upon which priority is claimed. Written description for 0-sulfation at C2 of iduronic acid units and N-sulfation and 0-sulfation at C2 of glucosamine units may be found in Figure 1, or for from about 50% to about 100% of primary hydroxyls in glucosamine residues and secondary hydroxyl groups in disaccharide units are substituted by 0-sulfate esters in paragraph 29 on page 9, lines 26-28, however no support is found for "O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units", which is a broader scope than the disclosed structure in Figure 1 and more specific than the genus disclosed in the specification in paragraph 29 on page 9, lines 26-28."

In response, Applicant has amended claim 1 to remove any reference to "vertexes" in claim 1 and that the limitation of "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction" is supported in the specification as follows.

Par. [0022] beginning on page 6, line 22 of the specification recites: "UFH is a complex polysaccharide composed of repeating disaccharides of uronic acid → glucosamine (see Figure 1 for a sample structure of a heparin constituent). The disaccharide units may be biosynthetically modified, for example, as N-acetyl or N-sulfate glucosamine, 2-O-sulfate uronic acid and 6-O-sulfate and/or 3-O-sulfate glucosamine.", which supports the claimed "the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction".

Methodology for performing the claimed O-sulfation is described in Par. [0030] beginning on page 10, line 15 of the specification. A working example illustrating methodology for performing the claimed O-sulfation is described in Par. [0062] beginning on page 22, line 10 of the specification.

Based on the preceding argument, Applicant respectfully requests that the rejection of claim 1 on the ground of allegedly failing to comply with the written description requirement under 35 U.S.C. § 112, first paragraph be withdrawn.

35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 2, 5 and 6 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner argues: "Amended claim 2 recites the limitation "the first anticoagulant reduction characteristic" in line 2. Amended claim 5 recites the limitation "the second anticoagulant reduction characteristic" in line 2. Amended claim 6 recites the limitation "the first anticoagulant reduction characteristic and the second anticoagulant reduction characteristic" in lines 2-3. There is insufficient antecedent basis for this limitation in the amended claims. New claim 91 depends from amended claim 1. Amended claim 1 recites "an anticoagulant reduction characteristic and an angiogenesis inhibition characteristic," not a first or second anticoagulant reduction characteristic... For the purpose of advancing prosecution, Examiner is interpreting amended claims 2, 5 and 6 as being drawn to the first and second anticoagulant reduction characteristic recited in new claim 93."

In response, Applicants have amended claims 2, 5, and 6 such that the amended claims 2, 5, and 6 depend from claim 93 instead of from claim 91.

Based on the preceding argument, Applicant respectfully requests that the rejection of claim 1 under 35 U.S.C. § 112, second paragraph be withdrawn.

35 U.S.C. § 102(b)

The Examiner rejected claims 1, 2, 5, 6, 43 and 91-94 under 35 U.S.C. § 102(b) as allegedly being anticipated by Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892).

Applicant respectfully contends that Naggi does not anticipate claim 1, because Naggi does not teach each and every feature of claim 1.

As a first example of why Naggi does not anticipate claim 1, Naggi does not teach the feature: "wherein the super-sulfated oxidized heparin fraction fully inhibits fibroblast growth factor (FGF2) induced angiogenesis".

Although Naggi teaches supersulfated heparins, Naggi's technique for generating the supersulfated heparins differs from Applicant's technique of generating the claimed super-sulfated oxidized heparin fractions. Specifically, Naggi teaches generating supersulfated heparins by a process of treating heparin with a mixture of sulfuric acid and chlorosulfonic acid (see Naggi, col. 4, lines 66-67), which markedly differs from Applicant's described process of O-sulfating a first oxidized heparin fraction (via sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction).

Therefore, it cannot be argued that any of Naggi's supersulfated heparins are the same as any of Applicant's super-sulfated oxidized heparin fractions that were demonstrated in Table 3 on page 29 of Applicant's specification as having the characteristic of fully inhibiting FGF2 induced angiogenesis. The scope of claim 1 does not include all super-sulfated oxidized heparin fractions that may potentially exist, but is specifically limited to those super-sulfated oxidized heparin fractions that fully inhibit FGF2 induced angiogenesis.

Applicant asserts that it cannot be argued that Naggi's supersulfated heparins fully inhibit FGF2 induced angiogenesis in the absence of proof by experimental or test results. Since such experimental or test results do not exist in Naggi, and since Naggi does not explicitly teach that that Naggi's supersulfated heparins fully inhibit FGF2 induced angiogenesis, Applicant maintains that Naggi does not teach the preceding feature of claim 1.

As evidence that Naggi did not teach fully inhibiting FGF2 induced angiogenesis though use of supersulfaction, Applicant cites Lars Lundin et al., Selectively Desulfated Heparin Inhibits Fibroblast Growth Factor-induced Mitogenicity and Angiogenesis, Journal of Biological Chemistry, Vol. 275, No. 32 (August 11, 2000), (hereinafter, "Lundin"), a copy of which was included in Appendix A of Applicant's office action response filed December 31, 2007. See Lundin's Abstract ("FGF-2 induced angiogenesis in chick embryos was inhibited by 6-O-desulfated heparein"). In contrast, Applicant is claiming sulfation of an oxygenated heparin fraction to inhibit FGF2 induced angiogenesis, which is the exact opposite of desulfation. In light of Lundin's teaching of desulfation for inhibiting angiogenesis which teaches the state of the art in year 2000 well after the date of 1988 when the Naggi patent was issued, it is clear that Naggi did not teach fully inhibiting FGF2 induced angiogenesis though use of supersulfaction. In light of Lundin's teaching of desulfation for inhibiting angiogenesis, Applicant asserts that Applicant's teaching that sulfation of an oxygenated heparin fraction (in the manner described in Applicant's specification and claimed in claim 1) totally inhibits FGF2 induced angiogenesis is an ***unexpected result*** that was not taught by Naggi in 1988.

In addition, the preceding feature of claim 1 distinguishes Naggi as follows. Applicant's specification in Paragraph [0005] beginning on page 2, line 16 states that it is known in the art that FGF2 induced angiogenesis plays a role in pathological angiogenesis associated with solid

tumors, diabetic retinopathy, and rheumatoid arthritis. Therefore, the capability of full inhibition of FGF2 induced angiogenesis by the super-sulphated oxidized ultra-LMWH of the present invention may be beneficially employed to inhibit accelerated angiogenesis for cancer cases in which a tumor secrets excess angiogenesis growth factors including FGF2, and also to inhibit angiogenesis associated with diabetic retinopathy and rheumatoid arthritis in which FGF2 is implicated, without affecting basal angiogenesis (i.e., normal or physiological angiogenesis) as characterized by the PBS control of Tables 3 and 4 on pages 29 and 30, respectively, of Applicant's specification as discussed *supra*. In contrast, Naggi is totally silent as to FGF2 induced angiogenesis and is totally silent as to the use of supersulfated heparind for treatment of cancer, diabetic retinopathy and rheumatoid arthritis, which is additional evidence that Applicant's super-sulfated oxidized heparin fraction is patentably distinct from Naggi's supersulfated heparins.

As a second example of why Naggi does not anticipate claim 1, Naggi does not teach the feature: "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction".

The Examiner argues that the chemical structure shown in Naggi, col. 6, lines 1-12, with m=4 and A=SO_3^- satisfies the preceding feature of claim 1.

In response, Applicant asserts that claim 1 requires the super-sulfated oxidized heparin fraction to have a chemical structure obtained by O-sulfating a first oxidized heparin fraction (via sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction). However, Naggi does not teach a process of O-sulfating a first oxidized heparin fraction (via

sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction). Rather, Naggi teaches generating supersulfated heparins by a process of treating heparin with a mixture of sulfuric acid and chlorosulfonic acid (see Naggi, col. 4, lines 66-67), which markedly differs from the preceding process recited in claim 1 and described in Applicant's specification.

Applicant acknowledges that Naggi would legally teach the preceding feature of claim 1 if the supersulfated heparins resulting from Naggi's process for generating supersulfated heparins have the same chemical structure as would result from implementing the process in claim 1 of O-sulfating a first oxidized heparin fraction (via sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction). However, Naggi does not teach that supersulfated heparins have the same chemical structure as Applicant's super-sulfated oxidized heparin fraction, as evidenced by the fact that none of Naggi's supersulfated heparins in Naggi's examples have the same chemical structure as any example of Applicant's super-sulfated oxidized heparin fractions appearing in Applicant's specification.

Therefore, it cannot be argued that the supersulfated heparins resulting from Naggi's process for generating supersulfated heparins have the same chemical structure as would result from implementing the process in claim 1 of O-sulfating a first oxidized heparin fraction (via sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction). Thus, it cannot be argued that the chemical structure shown in Naggi, col. 6, lines 1-12, with m=4 and A=SO_3^- would result from implementing the process in claim 1 of O-sulfating a first oxidized heparin fraction (via sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction).

Furthermore, the feature of the super-sulfated oxidized heparin fraction having "a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has

been O-sulfated by sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction" requires that the amount of sulfation present in the super-sulfated oxidized heparin fraction exceed the amount of sulfation present in the first oxidized heparin fraction. However, Naggi does not disclose that the amount of sulfation in Naggi's supersulfated heparins exceeds the amount of sulfation in a first oxidized heparin fraction.

Based on the preceding arguments, Applicant respectfully maintains that Naggi does not anticipate claim 1, and that claim 1 is in condition for allowance. Since claims 2, 5, 6, 43 and 91-94 depend from claim 1, Applicant contends that claims 2, 5, 6, 43, and 91-94 are likewise in condition for allowance.

In addition with respect to claims 93, 2, 5, and 6, Naggi does not teach the feature:

"wherein the anticoagulant reduction characteristic comprises a first anticoagulant reduction characteristic, a second anticoagulant reduction characteristic, or a combination thereof; wherein the first anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a mean percent inhibition of platelet clot strength by factor of at least about 8 relative to a mean percent inhibition of platelet clot strength of unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood; wherein the second anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a prolongation of clotting time of human blood by at least 75% relative to a prolongation of clotting time of human blood by unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood, subject to the clotting time being a prothrombin time (PT) or an activated partial thromboplastin time (APTT); and wherein the angiogenesis inhibition characteristic is that the oxidized heparin fraction in an endothelial cell (EC) growth medium cancels an effect of recombinant human fibroblast growth factor (FGF2) on EC tube formation in the EC growth medium under a condition of the concentration of FGF2 in the EC growth medium being sufficient to increase a

length or area of the EC tube formation by a factor of at least about 2 if the oxidized heparin fraction is not in the EC growth medium" (claim 93);

"wherein the anticoagulant reduction characteristic comprises the first anticoagulant reduction characteristic" (claim 2);

"wherein the anticoagulant reduction characteristic comprises the second anticoagulant reduction characteristic" (claim 5);

"wherein the anticoagulant reduction characteristic comprises the first anticoagulant reduction characteristic and the second anticoagulant reduction characteristic" (claim 6).

As to claims 5 and 93, the Examiner argues: "Naggi et al. discloses the reduction of the anticoagulation reduction characteristic with regards to the activated partial thromboplastin time (APTT) (column 9, lines 7-11 and 47-60), explicitly meeting the limitations of instant claims 5 and 93."

In response, Applicant notes that the data in the APTT column in TABLE 1 of Naggi, col. 9, lines 50-59 ***is not expressed in units of clotting time*** (or prolongation of clotting time) as is recited in claims 5 and 93, but rather ***is expressed in units of U/ml*** which is totally irrelevant to the preceding feature of claims 5 and 93. Naggi does not present any data that teaches the limitation in claims 5 and 93 of: "wherein the second anticoagulant reduction characteristic is that the oxidized heparin fraction reduces ***a prolongation of clotting time*** of human blood by at least 75% relative to a prolongation of clotting time of human blood by unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood, subject to the clotting time being a prothrombin time (PT) or an activated partial thromboplastin time (APTT)" (emphasis added).

As to claims 2 and 6, the Examiner argues: "Naggi et al. is silent as to an angiogenesis inhibition characteristic and the anticoagulant reduction characteristic in terms of a "percent inhibition of platelet clot strength," but does recite that the depolymerized and supersulfated heparin shows a weak

anticoagulant activity (column 5, lines 41-45). Therefore there is reason to believe that the characteristics recited in instant claims 2 and 6 are inherent in the compound disclosed by Naggi et al."

In response, Applicant respectfully contends that the Examiner's argument that Naggi recites that the depolymerized and supersulfated heparin shows a weak anticoagulant activity does not inherently teach the feature of "wherein the first anticoagulant reduction characteristic is that the oxidized heparin fraction reduces a mean percent inhibition of platelet clot strength by factor of at least about 8 relative to a mean percent inhibition of platelet clot strength of unfractionated heparin under a condition of the concentration of the oxidized heparin fraction in human blood being equal to the concentration of the unfractionated heparin in human blood". Applicant respectfully asserts that it cannot be concluded that the recited reduction of a mean percent inhibition of platelet clot strength by factor of at least about 8 is inherently taught by the existence of a weak anticoagulant activity.

Additionally as to claims 93, 2, 5, and 6, the Examiner does not even allege that Naggi teaches the feature: "wherein the angiogenesis inhibition characteristic is that the oxidized heparin fraction in an endothelial cell (EC) growth medium cancels an effect of recombinant human fibroblast growth factor (FGF2) on EC tube formation in the EC growth medium under a condition of the concentration of FGF2 in the EC growth medium being sufficient to increase a length or area of the EC tube formation by a factor of at least about 2 if the oxidized heparin fraction is not in the EC growth medium".

Accordingly, Naggi does not anticipate claims 93, 2, 5, and 6.

In addition with respect to claim 91, Naggi does not teach the feature: "wherein the super-sulfated oxidized heparin fraction comprises a sulfate to carboxylate ratio of about 5:1".

The Examiner argues that the chemical structure shown in Naggi, col. 6, lines 1-12, with m=4 and A=SO_3^- and B=SO_3^- satisfies the preceding feature of claim 91.

Applicant disagrees and requests that the Examiner explain how the chemical structure shown in Naggi, col. 6, lines 1-12, with m=4 and A=SO_3^- and B=SO_3^- allegedly teaches a sulfate to carboxylate ratio of about 5:1.

Accordingly, Naggi does not anticipate claim 91.

In addition with respect to claim 94, Naggi does not teach the feature: "forming the oxidized heparin fraction of claim 1, wherein said forming the oxidized heparin fraction comprises O-sulfating the first oxidized heparin fraction by performing sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction".

The Examiner argues: "Naggi et al. discloses the heparin treated with sulfuric acid and chlorosulfonic acid, a strong oxidizing agent, to depolymerize and super-sulfate heparin (spanning column 4 lines 66-68 and column 5 lines 1-10), meeting the instant limitations of instant claim 94 and addressing the term "oxidized heparin fraction." The instant specification recites, "The percentage of hydroxyl residues that are oxidized in accordance with the present invention is determined by the length of incubation with the oxidizing agent and/or the quantity of oxidizing agent used," on page 8, lines 24-26, and further recites non-limiting embodiments. The term "oxidized heparin fraction" does not require the hydroxyl residues of the oxidized heparin fraction to be present in the oxidized state, and the term "oxidized heparin fraction" encompasses heparin compounds wherein the hydroxyl residues are not oxidized as indicated by the limitation of instant claim 91, "wherein the sulfate to carboxylate ratio is about 5:1," as a sulfate to carboxylate ratio of 5:1 is possible only when the hydroxyl residues are present in the oxidation state of hydroxyl residues."

In response, Applicant respectfully contends that the preceding argument of the Examiner does not address the existence of the first oxidized fraction as opposed to the oxidized heparin that is generated by being O-sulfated. Claim 94 specifically recites O-sulfating the first oxidized fraction by performing sulfate substitution at oxygen bonds within repeating units of the first oxidized heparin fraction.

Accordingly, Naggi does not anticipate claim 94.

In addition with respect to claim 43, Naggi does not teach the feature: "A composition comprising from about 60% to about 100% of the oxidized heparin fraction of claim 1, and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof".

The Examiner argues: "Naggi et al. recites "It is also generally recognized that at the same degree of polymerization, the biological activity of polysaccharides increases with their sulfation degree," (column 3, lines 42-44), which provides guidance to one of ordinary skill in the art to instantly envision said compound. Naggi et al. discloses the compound in the form of a pharmaceutical composition (column 10, lines 55-57), meeting the limitations of instant claim 43".

In response, Applicant respectfully contends that the preceding argument of the Examiner does not demonstrate that Naggi specifically teaches the claimed ranges of "from about 60% to about 100% of the oxidized heparin fraction of claim 1" and "from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof"

Therefore, Naggi does not anticipate claim 43.

35 U.S.C. § 103(a): Claims 1, 43, 49 and 50 (Naggi in view of Weitz)

The Examiner rejected claims 1, 43, 49 and 50 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Weitz et al. (US Patent 6,075,013, issued 13 Jun 2000, of record).

With respect to claims 1 and 43, the Examiner has not invoked Weitz as a reference as allegedly disclosing any feature specific to claim 1 or claim 43. The Examiner appears to rely on Naggi as allegedly disclosing all of the features of claim 1 and 43 based on the Examiner's prior arguments with respect to Naggi allegedly anticipating claims 1 and 43 by allegedly teaching all of the features of claims 1 and 43.

In response, Applicant relies on Applicant's arguments *supra* as to why Naggi does not teach or suggest all of the features of claims 1 and 43. Accordingly, Applicant maintains that claims 1 and 43 are not unpatentable over Naggi in view of Weitz. Moreover, since claims 49 and 50 depend from claim 1, Applicant maintains that claims 49 and 50 are not likewise unpatentable over Naggi in view of Weitz.

35 U.S.C. § 103(a): Claims 1 and 56-59 (Naggi in view of Conrad)

The Examiner rejected claims 1 and 56-59 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Conrad et al. (US Patent 5,280,016, issued 18 Jan 1994, cited in PTO-892).

With respect to claim 1, the Examiner has not invoked Conrad as a reference as allegedly disclosing any feature specific to claim 1. The Examiner appears to rely on Naggi as allegedly disclosing all of the features of claim 1 based on the Examiner's prior arguments with respect to Naggi allegedly anticipating claim 1 by allegedly teaching all of the features of claim 1.

In response, Applicant relies on Applicant's arguments *supra* as to why Naggi does not teach or suggest all of the features of claim 1. Accordingly, Applicant maintains that claim 1 and is not unpatentable over Naggi in view of Conrad. Moreover, since claims 56-59 depend from claim 1, Applicant maintains that claims 56-59 are not likewise unpatentable over Naggi in view of Conrad.

35 U.S.C. § 103(a): Claims 1, 43 and 51-54 (Naggi, in view of Conrad and Kerbel)

The Examiner rejected claims 1, 43 and 51-54 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Conrad et al. (US Patent 5,280,016, issued 18 Jan 1994, cited in PTO-892) as applied to claims 1 and 56-59 above, and further in view of Kerbel et al. (Cancer and Metastasis Reviews, 2001, 20, p79-86, cited in PTO-892).

Since claims 43 and 51-54 depend from claim 1, which Applicants have argued *supra* to not be unpatentable over Naggi in view of Conrad, Applicant maintains that claims 43 and 51-54 are likewise not unpatentable over Naggi in view of Conrad and further in view of Kerbel under 35 U.S.C. §103(a).

35 U.S.C. § 103(a): Claims 1, 56, 61 and 62 (Naggi in view of Scholander)

The Examiner rejected claims 1, 56, 61 and 62 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Naggi et al. (US Patent 4,727,063, issued 23 Feb 1988, cited in PTO-892) in view of Scholander (US Patent 6,461,665, issued 08 Oct 2002, of record).

With respect to claim 1, the Examiner has not invoked Scholander as a reference as allegedly disclosing any feature specific to claim 1 and therefore appears to rely on Naggi as allegedly disclosing all of the features of claim 1 based on the Examiner's prior arguments with respect to Naggi allegedly anticipating claim 1 by allegedly teaching all of the features of claim 1.

In response, Applicant relies on Applicant's arguments *supra* as to why Naggi does not teach or suggest all of the features of claim 1. Accordingly, Applicant maintains that claim 1 and is not unpatentable over Naggi in view of Scholander. Moreover, since claims 56-59 depend from claim 1, Applicant maintains that claims 56-59 are not likewise unpatentable over Naggi in view of Scholander.

CONCLUSION

Based on the preceding arguments, Applicant respectfully believes that all pending claims and the entire application meet the acceptance criteria for allowance and therefore request favorable action. If the Examiner believes that anything further would be helpful to place the application in better condition for allowance, Applicant invites the Examiner to contact Applicant's representative at the telephone number listed below. The Director is hereby authorized to charge and/or credit Deposit Account 19-0513.

Date: 08/11/2008

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